UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/701,236	11/04/2003	Brenda F. Baker	ISIS-5207	5280

32650 7590 04/02/2009

WOODCOCK WASHBURN LLP
CIRA CENTRE, 12TH FLOOR
2929 ARCH STREET
PHILADELPHIA, PA 19104-2891

EXAMINER	
VIVLEMORE, TRACY ANN	
ART UNIT	PAPER NUMBER
1635	

MAIL DATE	DELIVERY MODE
04/02/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/701,236	BAKER ET AL.	
	Examiner	Art Unit	
	Tracy Vivlemore	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 71-79* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 71-79* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/1/08, 11/6/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Any rejection or objection not reiterated in this Action is withdrawn.

Double Patenting

The obviousness-type double patenting rejections over copending application numbers 10/700,697, 10/701,264 and 10/701,316 are withdrawn in view of the terminal disclaimers filed January 12, 2009.

Claim Rejections - 35 USC § 103

Claims 1 and 71-79 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al. (Cell 1993), Manche et al. (Molecular and Cellular Biology 1992), Agrawal et al. (WO 94/01550, cited on IDS of 4/4/05) Baracchini et al. (US 5,801,154) and Acevedo et al. (US 5,519,134).

The claims are directed to compositions comprising a duplex of non-linked strands 12 to 30 linked nucleotides in length at least one strand comprises a plurality of 2'-hydroxyl pentofuranosyl sugars and each strand comprises a modified nucleoside comprising a sugar surrogate. Specific embodiments recite that the compound comprises a phosphorothioate linkage or recite particular sugar surrogates.

At the time the invention was made short duplex RNAs with complementarity to a gene were known to those of ordinary skill in the art and were synthesized for a variety of purposes such as study of enzyme structure and regulation of gene expression.

Lee et al. teach that lin-4 is a gene essential for the normal temporal control of postembryonic developmental events in *C. elegans* that acts by negatively regulating the level of LIN-14 protein. Lee et al. further teach that the lin-4 gene transcribes two different products, one of which forms a stem-loop duplex structure with imperfect complementarity with lin-14 mRNA, suggesting that lin-4 regulates lin-14 translation via an antisense RNA-RNA interaction. Lee et al. do not teach duplexes with perfect complementarity to a gene and do not teach the use of modified nucleotides such as 2'-OMe and 2'-F.

Manche et al. teach that the protein kinase DAI, the double-stranded RNA-activated inhibitor of translation, is a pivotal cellular regulatory enzyme that is an important element in the host antiviral response. Despite its importance as a regulatory enzyme, the interactions between DAI and its RNA effectors were complicated and incompletely understood. To better understand these interactions Manche et al. analyzed interaction of the enzyme with RNA duplex molecules of specified sizes ranging from 15-104 nt (see figure 1) in order to study binding and protection of dsRNA as well as activation and inhibition of the kinase.

Agrawal et al. teach self-stabilized oligonucleotides comprising a target hybridizing region and a self-complementary region. On page 15 Agrawal et al. teach that the self-complementary region of the oligonucleotide is fully or partially

complementary to the hybridizing region while at page 9, line 30 through page 10 line 1 they teach that the target hybridizing region is complementary to a nucleic acid sequence from a variety of sources including viruses, pathogens, cellular genes or gene transcripts. On page 8 Agrawal et al. teach that the self-stabilized oligonucleotides are composed of ribonucleotides, deoxynucleotides and/or modified nucleotides. Page 15 and 16 describe embodiments where the oligonucleotide is a single nucleic acid strand that forms a double stranded structure as well as an embodiment where the self-complementary region is connected to the hybridizing region by a non-nucleotide linker, making the self-complementary region and the hybridizing region two separate complementary nucleic acid strands. On pages 17, line 27 through page 18 Agrawal et al. teach that the self-stabilized oligonucleotides can be administered to the cells of an animal to inhibit gene expression in the animals.

At the time the instant application was filed those of ordinary skill in the art were familiar with antisense oligonucleotides used for research purposes and for inhibition of gene expression. The teachings of Baracchini et al. are representative of knowledge of modified nucleic acids from the antisense art. Although it is acknowledged that antisense oligos inhibit expression via a different mechanism, Baracchini et al. provide a template of known modifications and screening methods that form a basis for stabilization of duplex RNA structures. Baracchini et al. teach that preferred oligonucleotides are modified in their sugar, backbone linkage and nucleobase composition and that such modifications are desirable in antisense oligonucleotides because these modifications have desirable properties such as enhanced cellular

uptake, enhanced affinity for nucleic acid targets and increased stability in the presence of nucleases. The modified oligonucleotides described at columns 6-7 include morpholino, cyclobutyl and peptide nucleic acid substitutions.

Other modified sugars were known to those in the art at the time the instant application was filed. Acevedo et al. teach pyrrolidine-based monomers suitable for incorporation into any position of a nucleic acid oligomer and provide synthetic schemes for converting a pyrrolidine structure into a phosphoramidite suitable for automated synthesis.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make short duplex RNAs that comprise modified nucleotides. Lee et al. and Agrawal et al. teach inhibition via duplex RNAs and Manche et al. teach that short duplex RNAs had uses in the study of enzyme binding. Based on the knowledge available to the person of ordinary skill of the ways to incorporate modified nucleotides as taught by Baracchini et al. and Acevedo et al. and the usefulness of modified nucleotides in providing nuclease stability and binding affinity that is provided by the antisense art, the person of ordinary skill would be motivated to use these known modifications and modification patterns as a starting point for optimizing the stability and affinity of short duplex RNAs. The person of ordinary skill in the art would be able to predictably make duplex RNA sequences comprising the claimed modifications because these modifications are well known and routinely used by those in the art.

Thus, the invention of claims 1 and 71-79 would have been obvious, as a whole, at the time the invention was made.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tracy Vivlemore whose telephone number is (571)272-2914. The examiner can normally be reached on Mon-Fri 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz, can be reached on 571-272-0763. The central FAX Number is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file

folder(s) as well as general patent information available to the public. For more information about the PAIR system, see http://pair-direct.uspto.gov.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Tracy Vivlemore
Primary Examiner
Art Unit 1635

/Tracy Vivlemore/
Primary Examiner, Art Unit 1635